

### **REMARKS / ARGUMENTS**

The Non-Final Office Action mailed November 22, 2006, was received and reviewed. Claims 1 through 34 are pending in the Application, and claims 1 through 15 are withdrawn from consideration as being directed to a non-elected invention. Claims 16 through 34 were rejected.

Applicants gratefully acknowledge the withdrawal of the rejection of claims 30 and 34 under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph for alleged indefiniteness, and the withdrawal of the rejection of claims 16-34 under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, as being based upon a specification that allegedly provides insufficient written description of the claimed invention.

Applicants respectfully request reconsideration of the Application by the Examiner in view of the amendments provided in response to the newly raised rejections, and in further view of following remarks and arguments.

### **CLAIM AMENDMENTS**

Claims 1-3, 5, 6, 11, 12, 14-16, and 18-26 are being amended as shown. In particular, claims 1-3, 5, 6, 11, 12, 14, 18-20 and 24-26 have been amended by the insertion of the term “non-human” before the word “organisms” at every occurrence of the word “organisms,” throughout the claims. Claims 2, 16, 21, 22 and 23 are being amended to correct informalities in the language, such that expression cassettes of these claims are uniformly described as “directing the expression of” chimeric RNA transcripts, and are expressly mentioned when present on the expression vectors of claims 16, and 21-23.

These amendment(s) should be entered into the record because they neither add new matter to the Application, nor raise any new issues that would require further search. Furthermore, these amendments place the claims in condition for allowance, or, alternatively, in better condition for appeal.

## THE REJECTIONS

### 35 USC § 101:

Claims 18-20, 24-26, and 31-34 stand rejected under 35 USC § 101, as allegedly being directed to non-statutory subject matter. According to the Office Action of 11/22/2006 the broadest reasonable interpretation of independent claim 18 includes a kit that comprises a human being. Claim 19-20, 24-26, and 31-34 are all dependent upon claim 18, and thus rejected for the same reason.

As suggested by the Examiner (on page 3 of the Office Action), the claims have been amended by inserting the term “non-human” before the word “organisms,” wherever this word appears in the claims, thereby rendering the rejection under 35 USC § 101 for claims to non-statutory subject matter moot. Consequently, Applicants respectfully request that the rejection of claims 18-20, 24-26, and 31-34 under 35 USC § 101, be rescinded.

### 35 USC § 103(a) – Obviousness:

Claims 16-34 stand rejected under 35 U.S.C. § 103(a), for allegedly being unpatentable over Sijen *et al.* (2001) *Cell* 107:465-476; Pal-Bhadra *et al.* (1998) *Cell* 99:35-46; Voinnet *et al.* (1998) *Cell* 95:177-187; Fire *et al.* (1990) *Gene* 93:189-198; Kennerdell *et al.* (1998) *Cell* 95:1017-1026; and Elbashir *et al.* (2001) *Nature* 411:494-498. Applicants respectfully traverse this rejection because the Examiner has failed to establish a *prima facie* case of obviousness. Furthermore, it is clear from the Office Action of 11/22/2006, that the Examiner has employed “hindsight reconstruction” to arrive at the claimed invention from the six prior art references cited.

### What is required to establish a *prima facie* case of obviousness?

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

MPEP § 2143, 8<sup>th</sup> Ed., Rev. 5, Aug. 2006, p. 2100-126.

As will be shown below in the arguments below, in instant case the first and third criteria described above have not been met.

**To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations.**

MPEP § 2143.03 specifically instructs:

To establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

MPEP § 2143.03, 8<sup>th</sup> Ed., Rev. 5, Aug. 2006, p. 2100-131.

The principle pending independent claim at issue in the present Application is claim 16. Before considering this list of critical limitations of this claim, it would be instructive to step back and reflect on the purpose of the kit of claim 16, and, more generally, of the claimed invention as a whole. As described in detail in the specification, the instant invention provides methods and kits for altering levels of expression of a plurality of gene products by the process of RNA interference, which is induced by a specific "universal interfering RNA" that is directed towards and specifically targets a commonly-shared "universal target RNA" which is borne by a plurality chimeric RNA transcripts, at least two of which also bear subject RNAs that encode gene products whose expression is to be reduced. *Specification, e.g., Summary of Invention*, pp. 7-14.

Regarding the pending claims at issue, independent claim 16 is specifically directed towards kits for practicing the methods of the invention. As amended above, it reads:

Claim 16: A kit comprising, in a compartmentalized carrier:

a plurality of expression vectors each comprising an expression cassette that directs the expression of a chimeric RNA transcript that has a subject RNA operably linked to a universal target RNA, wherein the expression cassettes of at least two of the plurality of expression vectors direct the expression of chimeric RNA transcripts with different subject RNAs, and wherein the expression cassettes of all of said plurality of expression vectors direct the expression of chimeric RNA transcripts with the same universal target RNA; and

a universal interfering RNA targeting said universal target RNA, or an interfering RNA transcription vector that directs the expression of said universal interfering RNA,

wherein said universal interfering RNA is an siRNA or shRNA.

Accordingly, the critical limitations of claim 16, many of which are shared with the only other pending independent claim (i.e., claim 18), are thus:

1. **a plurality of expression vectors comprising an expression cassette;**
2. wherein each expression cassette directs the expression of a **chimeric RNA transcript;**
3. wherein said chimeric RNA transcript has **a subject RNA** operably linked to **a universal target RNA;**
4. wherein **at least two chimeric RNA transcripts bear different subject RNAs;**
5. wherein **all chimeric RNA transcripts bear the same universal target RNAs;**
- and
6. either (a) **a universal interfering RNA targeting said universal target RNA,** or (b) an expression vector that directs the expression of said universal interfering RNA; and
7. wherein **said universal interfering RNA is either (a) an siRNA or (b) an shRNA.**

Turning now to the six references cited by the Examiner in the Office Action of 11/22/2006, Applicants respectfully assert that a limitation of independent claims 16 & 18 that is neither taught nor suggested by any of the six references is a **universal interfering RNA** that specifically targets a universal target RNA present on all of a plurality of chimeric RNA transcripts encoding different subject RNAs and induces RNA interference to alter (i.e., reduce) the expression of the gene products encoded by the subject RNAs. Indeed, over the course of almost five pages of discussion regarding the six prior art references cited (Office Action, pp. 5-9), the Examiner has failed to identify where such a universal interfering RNA is specifically taught or suggested. Additionally, throughout this discussion the Examiner has generally failed to procedurally follow the recommendation of the MPEP § 706.02(j), which instruct the Examiner to set forth in the Office Action “the difference or differences in the claim over the applied reference(s), ... the proposed modification of the applied reference(s) necessary to arrive at the claimed subject matter, and ... an explanation why one of ordinary skill in the art at the time the invention was made would have been motivated to make the proposed modification.

To be fair, in his discussion of Sijen *et al.* (Sijen *et al.*, *Cell* 107:465-476 (2001)) the Examiner alleges that “Sijen *et al.* demonstrate how a single interfering dsRNA can inhibit the expression of at least three different, non-naturally occurring transcripts, and at least two different subject RNAs linked to a common target, GFP” (Office Action, p. 6, 2<sup>nd</sup> ¶). The Examiner then suggests that Sijen *et al.* therefore teaches or suggests a universal interfering RNA. However, as a first matter, Applicants note that the “single interfering dsRNA” of Sijen *et al.* referred to by the Examiner, is not a universal interfering RNA in accordance with the universal interfering RNA of claims 16 and 18, because it is neither an siRNA nor an shRNA, as required by the claims. Moreover, a careful reading of Sijen *et al.* reveals that, contrary to the assertion of the Examiner, in the experiments depicted in Figure 3, GFP does not serve as the target. Instead, GFP serves as a bioluminescent reporter, while *lacZ* serves as the target of the illustrated “dsRNA triggers.” Additionally, Applicants note that the chimeric transcript represented by pSAK4 in Figure 3 is not a “chimeric RNA transcript” in accordance with the chimeric RNA transcripts of claims 16 and 18, because it does not contain the *lacZ*

coding sequence which is the target of the depicted “dsRNA triggers.” Conversely, in the experiments depicted in Figure 4, GFP generally serves as the target of the majority of the identified dsRNA triggers, while *unc22Z* serves as a phenotypic reporter. As such, *unc22Z* may be considered to represent a “subject RNA” in the same sense as the subject RNA of claims 16 and 18. However, the collection of chimeric transcripts depicted in Figure 4 do not fall within the scope of the chimeric RNA transcripts of the claimed invention because the chimeric RNA transcripts of Figure 4 all bear the same subject RNA (i.e., *unc22Z*).

While the differences between the teachings of Sijen *et al.* and the limitations of independent claims 16 and 18 may, in hindsight, appear subtle, they are nonetheless significant. Further, no matter how the experimental systems of Sijen *et al.* are interpreted, it is clear that Sijen *et al.*, fails to teach that a single siRNA or shRNA directed to a target within any chimeric transcript can serve to knock down the expression of a plurality of chimeric RNA transcripts bearing that same target sequence. Thus, Sijen *et al.* (as well as the other five cited references) fails to teach the concept, element or limitation of the **universal interfering RNA** of pending claims 16 and 18, and fails to provide any embodiment of such a **universal interfering RNA**.

**To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings:**

MPEP § 2143.01 specifically instructs:

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so. *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006). ... The teaching, suggestion, or motivation must be found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. “The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to

those of ordinary skill in the art.” *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000).

MPEP § 2143.01, 8<sup>th</sup> Ed., Rev. 5, Aug. 2006, p. 2100-127.

Although, as explained *supra*, the combination of all six prior art publications cited in the Office Action of 11/22/2006 do not teach every element or limitation of the claimed invention, even if they did, Applicants respectfully assert that the teaching, suggestion or motivation to combine these references is absent either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. Furthermore, although the Examiner asserts in his brief discussion of motivation that skilled artisans would have been “motivated to make and test several different configurations of transgenes and vectors encoding chimeric transcripts, and to arrange such constructs in an organized fashion, compartmentalized as per normal laboratory practice, in well-marked containers, wells, test tubes, microtiter plates and so on....”, he alleges only that the source of the motivation would be to “define the particular molecular requirements of transitive RNAi in any given organism.” Office Action of 11/22/2006, p. 10, 2<sup>nd</sup> ¶.

In response, Applicants first note that kits of claims 16 and 18 have considerably broader application than to “define the particular molecular requirements of transitive RNAi.” Indeed, the kits of claims 16 and 18 can be used to induce the silencing of a plurality of gene products encoded by subject RNAs in cells and organisms that do not exhibit transitive RNAi, as explained in detail in the specification (*see, e.g., Specification* p. 23, l. 18 through p. 25, l. 4, and Figures 3 and 4). Applicants further assert that the Examiner’s assertions that the motivation to combine the references for the study of transitive RNAi, is not relevant to the problem to be solved by the claimed invention, which is generally outlined in the Specification in the Summary of Invention at pages 7 through 14.

Also, while the Examiner has suggested that one of skill in the art may have been motivated to combine the teachings of the cited references to “define the particular molecular requirements of transitive RNAi,” or to define the mechanisms behind transitive RNAi, Applicants respectfully assert that (a) there are several reasons that

skilled artisans would have been motivated to not combine the teachings of the six references, and (b) the assertions of the Examiner regarding such motivations are simply conclusory statements, which provide evidence of impermissible hindsight reconstruction of the claimed invention from elements picked and chosen from the prior art.

Aside from the conclusory statements regarding artisans studying the phenomenon of transitive RNA interference which are provided as evidence for the motivation to combine references, Applicants respectfully note that the Office Action of 11/22/2006 is procedurally defective, because the Examiner has failed to specifically identify where, either in the cited references themselves, or in the knowledge generally available to one of ordinary skill in the art, the suggestion or motivation to modify or combine the cited references to arrive at the claimed invention can be found.

Regarding the six cited references themselves, Applicants make the following observations:

Sijen *et al.* (*Cell* 107:465-476 (2001)), as noted *supra*, fails to demonstrate that siRNAs and shRNAs can be used to induce RNA interference-mediated destruction of any of the chimeric transcripts they employed in their studies. Sijen *et al.* also fails to teach that the expression of different subject RNAs can be subjected to RNA interference induced by a universal interfering siRNA or shRNA that targets a commonly-shared target RNA on a plurality of subject RNAs.

Neither Pal-Bhadra *et al.* (*Cell* 99:35-46 (1998)), which describes transitive gene silencing in *Drosophila*, nor Voinnet *et al.* (*Cell* 95:177-187 (1998)), which reports transitive silencing of a GFP transgene in plants, provide any teachings relevant to the claimed invention, because neither reference pertains to RNA interference-induced gene silencing. As stated in Pal-Bhadra *et al.*, “[t]he evidence indicates a process distinct from one involving RNA-mediated silencing ....” Pal-Bhadra *et al.*, p. 35, right column, ll. 41-42. As stated in Voinnet *et al.*, “[h]ere we describe how systemic PTSG can be induced following localized delivery of DNA.... These systems ... show that systemic gene silencing can be initiated from a small group of cells by an interaction of the introduced DNA with the corresponding target gene.” Voinnet *et al.*, p. 177, right column, ll. 26-31.

As noted in the Office Action of 11/22/2006, Fire *et al.* (*Gene* 93:189-198 (1990)) disclose a modular set of *lacZ* fusion vectors for studying gene expression and subcellular

localization of gene expression products in *C. elegans*. However, nowhere within this reference is there any discussion of using these vectors to reduce the expression of the transgenes or transgene fusions to be cloned into these vectors. Similarly, nowhere is there any discussion of RNA interference of the vector-borne transgenes or transgene fusions induced by a universal interfering RNA. Of course, the latter would not be expected, since this reference was published more than 7 years prior to the first description of RNA interference in *C. elegans* by Andy Fire and Craig Mello (*see Fire et al., Nature* 391:806-811 (1998)).

Kennerdell *et al. Cell* 95:1017-1026 (1998) disclose that long dsRNAs (of an average length of 1, 160 bp) corresponding to the coding sequences of the *frizzled* (*fz*) and *Drosophila frizzled2* (*Dfz2*) genes of *Drosophila* can be used to knock down the expression of these two gene products and thereby produce defects in embryonic patterning that mimic loss of *wingless* function. Although Kennerdell *et al.* discovered and disclosed that dsRNAs corresponding to coding sequences shared by the native *fz* and *Dfz2* transcripts “had weak but significant interfering activities [on the non-corresponding transcript],” (p. 1022, right column, l. 16), they specifically note that because of the genetic redundancy inherent between the *fz* and *Dfz2* genes, “injection of multiple dsRNAs [i.e., one dsRNA directed towards the *fz* transcript, and another dsRNA directed towards the *Dfz2* transcript] into a single animal, ..., might be a simple means to overcome this redundancy and generate mutant phenotypes.” Kennerdell *et al.*, p. 1023, left column, ll. 35-39, emphasis added.. Applicants further note that while Kennerdell *et al.* suggested that it might be possible to target two naturally-occurring transcripts for RNAi-induced silencing using a single dsRNA directed towards a sequence shared between two naturally-occurring transcripts, as mentioned by the Examiner, Kennerdell *et al.* basically teach away from this practice (and the claimed invention) by stressing that two distinct dsRNAs (i.e., one dsRNA directed towards the *fz* transcript, and another dsRNA directed towards the *Dfz2* transcript) had to be injected in order to produce the *wingless* phenotype, because the expression of both the *fz* and *Dfz2* genes had to be knocked down to overcome the redundancy of gene function and thereby generate the phenotype.

Finally, while Elbashir *et al.* (*Nature* 411:494-498 (2001)) do “teach the advantages, synthesis, and use of siRNAs in general for mediating gene-specific inhibition in flies and mammalian cells,” and “teach in general that RNAi is an effective tool for studying gene function,” as asserted on page 9 of the Office Action, Applicants respectfully note that Elbashir *et al.* teach (in Figures 1 and 2) that three distinct siRNA duplexes are required to efficiently silence the expression of three different luciferase reporter genes. In fact, Elbashir *et al.* even teach (in Figures 1 and 2) that two distinct siRNA duplexes are required to efficiently silence the expression of two sequence variants of the same firefly luciferase (i.e., GL2 & GL3) that share 95% sequence identity. See Elbashir *et al.*, p. 495, Figures 1 and 2. Elbashir *et al.* also teaches that “[t]he siRNA duplexes only reduced the expression of their cognate reporter gene, while the longer dsRNAs strongly and nonspecifically reduced reporter-gene expression.” Elbashir *et al.*, p. 496, ll. 29-32, emphasis added. Thus, Elbashir *et al.* teaches that (a) transcripts from transgenes that differ in sequence identity by as little as 5% can only be efficiently targeted for RNAi-induced silencing by specific cognate siRNAs that match the sequence of the target region of the specific transgene to be silenced, and (b) three different transgenes require three different siRNAs for efficient silencing. Consequently, Elbashir *et al.* also teaches away from the instant invention, which, in every embodiment, employs a single “universal interfering RNA” to induce RNAi-mediated silencing of a plurality of transgenes.

**The use of “hindsight reconstruction” to arrive at a finding of obviousness is impermissible.**

The U.S. Court of Appeals for the Federal Circuit has ruled:

It is impermissible to use the claimed invention as an instruction manual or “template” to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that “[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.” *In re Fritch*, 972 F.2d 1260, 23 USPQ 2d 1780, 1784 (Fed. Cir. 1992) (quoting *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988)).

Applicants respectfully assert that, in the Office Action mailed 11/22/2006, the Examiner has clearly picked and chosen among isolated disclosures in the prior art to deprecate the claimed invention. Evidence of this practice can be found in the fact that the Examiner has chosen to cite Elbashir *et al.* (*Nature* 411:494-498 (2001)) for its teachings on “the advantages, synthesis, and use of siRNAs in general for mediating gene-specific inhibition in flies and mammalian cells,” while ignoring the fact that Elbashir teaches that each of the three transgenes expressing a luciferase reporter protein studied must be targeted with a distinct siRNA that corresponds to the sequence of the transcript encoding that luciferase reporter protein. Further evidence of the Examiner’s picking and choosing from the cited art, can be found in the Examiner’s misinterpretation of the role played by the GFP-coding sequence in the experiments depicted in Figure 3 of Sijen *et al.* (*Cell* 107:465-476 (2001)), as discussed, *supra*.

Also, while MPEP § 2145(V) indicates that “[r]eliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention,” Applicants note that in order to attempt to build a *prima facie* case of obviousness, the Examiner has found it necessary to cite six references, which, when combined still fail to teach or suggest all of the limitations and elements of claims 16 and 18. Certainly, the Examiner’s use of six references to attempt to build a case of obviousness suggests the need to pick and choose potential claim limitations from the prior art, which, as noted above, has been explicitly forbidden by the Federal Circuit in In re Fine (837 F.2d 1071, 1075, 5 USPQ 2d 1596, 1600 (Fed. Cir. 1988)).

**In re Werner Kotzab, 217 F.3d 1365 (Fed. Cir. 2000) is instructive and further suggests that a proper *prima facie* case of obviousness has not been made.**

In considering the rejection of claims 16-34 under 35 U.S.C. § 103(a), for allegedly being unpatentable for obviousness, Applicants respectfully direct the Examiner to the highly relevant decision of the United States Court of Appeals for the Federal Circuit in In re Werner Kotzab, 217 F.3d 1365 (Fed. Cir. 2000), 55 U.S.P.Q.2d 1313 (hereinafter Kotzab).

Kotzab was an appeal to the Federal Circuit from the final decision of the Board of Patent Appeals and Interferences (Board) holding claims 1-10 in reexamination

number 90/004,441 unpatentable for obviousness under 35 U.S.C. § 103(a). The invention at issue involved an injection molding method for forming plastic articles. In such methods, the temperature of the mold must be controlled so that the injected plastic can cool and harden uniformly throughout the mold. Kotzab was confronted with the problem of providing optimal temperature control for an injection molding method to ensure the quality of the final product on the one hand, and achieving optimally short molding cycle times on the other hand. In such methods the temperature of various parts of the mold is controlled by using sensors to control the pulsing or flow of a temperature control medium (coolant) through channels within the mold.

Kotzab's claim 1, which is exemplary, reads, in part:

1. An improved method of controlling the temperature of an injection mold ..., the improvement comprising: controlling, via a single sensor, a plurality of flow controlling valves for the temperature controlling medium .... Id. at 1367.

During the reexamination proceedings, amended claims were finally rejected by the Examiner, and Kotzab appealed the rejections to the Board. The Board affirmed the Examiner's rejection, and provided additional comments, primarily for emphasis. Specifically, the Board agreed with the Examiner that WO 92/08598 ("Evans") discloses a process of controlling the temperature of an injection mold by using a sensor to control the pulsing of a temperature control medium through the mold. Moreover, the Board found, as explained by the Examiner, that Evans disclosed in a less preferred embodiment, using only one temperature measurement to control the coolant pulses rather than an average temperature measurement. Id. at 1368.

Kotzab filed a request for reconsideration, which the Board denied. In that decision, the Board reiterated agreement with the Examiner that it would have been obvious to one of ordinary skill in the art to utilize only one temperature measurement to control the coolant pulses in light of the Evans disclosure. Kotzab appealed the Board's decision to the Federal Circuit, resulting in the decision which is provided herewith as Exhibit A.

In Kotzab, the Federal Circuit reviewed the Board's ultimate determination of obviousness de novo. However, they also reviewed the Board's underlying factual findings for substantial evidence, since the ultimate determination of whether an

invention would have been obvious under 35 U.S.C. § 103(a) is a legal conclusion based on underlying findings of fact.

In their analysis of the facts at hand, the Federal Circuit first observed:

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. ... Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.” ... Kotzab at 1369.

Further, the Federal Circuit noted:

Most if not all inventions arise from a combination of old elements. ... Thus, every element of a claimed invention may often be found in the prior art. ... However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. ... Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. .... Id. at 1369-1370.

The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases, the nature of the problem to be solved. .... In addition, the teaching, motivation or suggestion may be implicit from the prior art as a whole, rather than expressly stated in the references. .... The test for an implicit showing is what the combined teachings, knowledge or one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art. .... Id. at 1370.

The Federal Circuit further held: “Whether the Board relies on an express or an implicit showing, it must provide particular findings thereto. See Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617. **Broad conclusory statements standing alone are not “evidence.”** *Id.* Kotzab at 1370, emphasis added.

Furthering their analysis, the Federal Circuit pointed out:

Kotzab’s primary argument that the Board erred in holding claims 1-10 unpatentable under 35 U.S.C. § 103(a) over Evans, or Evans in view of

secondary references, is that Evans does not teach or suggest the use of a single temperature sensor to control the plurality of flow control valves. Id. at 1370, emphasis added.

And it was on this point that the Federal Circuit agreed with Kotzab.

After considerable analysis on the relative meanings of the terms “sensor” and “system,” the Federal Circuit finally concluded:

In this case, the Examiner and the Board fell into the hindsight trap. The idea of a single sensor controlling a plurality multiple valves, as opposed to multiple sensors controlling multiple valves, is a technologically simple concept. With this simple concept in mind, the Patent and Trademark Office found prior art statements that in the abstract appeared to suggest the claimed limitation. But, there was no finding as to specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of Kotzab’s invention to make the combination in the manner claimed. In light of our holding of the absence of a motivation to combine the teachings in Evans, we conclude that the Board did not make out a proper *prima facie* case of obviousness in rejecting claims ... under 35 U.S.C. § 103(a) over Evans. Id. at 1371.

Applicants submit that in the instant case, the idea of a single universal interfering RNA targeting a common universal target sequence on a plurality of chimeric RNA transcripts, as opposed to multiple interfering RNAs specifically targeting sequences unique to each target RNA to be silenced, is a technologically simple concept. Applicants further assert that, as in Kotzab, the Examiner has fallen into a hindsight trap, and with this simple concept in mind, has found prior art statements that in the abstract appear to suggest the claimed limitation of a universal interfering RNA as recited in the specification and pending claims 16 and 18. And, as asserted *supra*, Applicants see no finding in the Office Action of 11/22/2006 as to the specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of the present invention to make the combination in the manner claimed. Hence, in light of the absence of a motivation to combine the teachings of Sijen *et al.*, Pal-Bhadra *et al.*, Voinnet *et al.*, Fire *et al.*, Kennerdell *et al.*, and Elbashir *et al.*, Applicants respectfully conclude that the Examiner has failed to produce a proper *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Consequently, for the reasons outlined immediately above, in addition to all of the other reasons outlined *supra*, Applicants respectfully request that the Examiner rescind the rejection of claims 16-34 under 35 U.S.C. § 103(a).

### CONCLUSIONS

Claims 16 through 34 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact the undersigned via his direct office line at 801-883-3463.

Additionally, should either claim 16 or 18, or both, be found to be allowable, Applicant respectfully requests rejoinder and examination of withdrawn process (method) claims (i.e., claims 1-15), in accordance with the provisions of MPEP § 821.04.

A petition for a one-month extension of time for the filing of this response is being filed concurrently herewith. Provisions for the payment of the necessary fee have been made in the petition. Therefore, it is believed that no other extension of time, or any additional fees are due with this response. If this is incorrect, an extension of time as deemed necessary is hereby requested, and the Commissioner is hereby authorized to charge any appropriate fees, or credit any over payment, to Deposit Account no. **50-1627**.

Respectfully submitted,

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March 22, 2007

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